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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,231	08/08/2001	Patricia G. Spear	7853-239	3399

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EXAMINER	
WORTMAN, DONNA C	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/18/2002 10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/924,231	SPEAR ET AL.	
	Examiner	Art Unit	
	Donna C. Wortman, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2002 and 19 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claims 1-5 as originally filed remain pending and under examination.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising the HVEM polypeptides as instantly claimed, does not reasonably provide enablement for using pharmaceuticals comprising those polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected to use the invention commensurate in scope with those claims for reasons of record in rejecting claims 1-5 in the previous Office action.

In response to this rejection, Applicant has argued (1) that as of the effective filing date of the instant specification, one of skill in the art would appreciate that a pharmaceutical composition comprising a soluble HVEM could be used to block herpesvirus from infecting a cell and/or to inactivate herpesvirus replication; (2) that it was well established that soluble TNF receptors, of which HVEM is a family member, sequester the receptors' ligands and thus inhibit the ligands' biological function, and that soluble viral entry receptors block virus entry into a target cell and are useful in treating or preventing viral infection; (3) that strains of HSV1 and HSV2 are capable of binding and entering mammalian cells through HVEM; (4) that the region of HSV gD that binds to HVEM mediates the binding of gD to other cellular receptors; (5) that the expectations of one of skill in the art at the time of filing are borne out by post-filing date

evidence; (6) that MPEP 2164.07 points out what is required to support an asserted utility; (7) that MPEP 2164.01(c) states that any enabled use that would reasonably correlate with the entire scope of the claim is sufficient to preclude a rejection for nonenablement based on how to use, and has submitted a Declaration under 37 CFR 1.132 of Dr. Celniker, along with supporting documents, cited on PTO 1449, an initialed copy of which is attached.

Applicant's remarks, the Celniker Declaration, and the documents have all been considered but not found persuasive. With respect to points (1)-(5), the specification discloses only in general that HVEM polypeptide can be a part of a pharmaceutical composition, provides only *in vitro* examples, does not provide any basis for correlating those *in vitro* examples to *in vivo* use, and does not teach how to use a pharmaceutical composition comprising HVEM to achieve a beneficial result; neither Applicant's arguments, a Declaration, nor supporting documents can be relied upon to supply what the specification does not teach. With respect to point (6), it is noted that the rejection was made under 35 USC 112, first paragraph, as failing to teach how to use, and not under 35 USC 101 as lacking a credible utility. With respect to point (7), claims drawn to the HVEM polypeptide *per se* have not been rejected for nonenablement based on how to use; claims drawn to a pharmaceutical composition comprising the polypeptide are rejected.

The Celniker Declaration has been carefully considered as well. The Declaration states, at pages 2-3, paragraph 5, that "... one of ordinary skill in the art at the time the earliest parent of the '231 application was filed would recognize that an exogenous

HVEM molecule which sequesters herpes virus from binding to cellular HVEM and thus interferes with the ability of herpes virus to infect cells could be formulated into a pharmaceutical composition for therapeutic or prophylactic use against herpes virus" and that "pharmaceutical formulations are taught in the specification" and are well known in the art as shown in Exhibit 2. The Declaration further states that Exhibit 3 establishes that a soluble receptor of the TNF receptor family inhibits the biological activity of its ligand; that Exhibit 4 demonstrates that a soluble form of a TNF receptor in the form of a fusion protein with an IgG inhibits TNF activity *in vivo* and *in vitro*; that Exhibit 5 describes using a soluble CD4-IgG to block HIV-1 infection in chimpanzees; that Exhibit 6 describes experiments in which two soluble forms of ICAM-1 block human rhinovirus binding and infection *in vitro*; concludes that recombinant HVEM would bind to and sequester HSV1 particles and prevent their binding to cellular HVEM and other cellular receptor, thus preventing HSV1 infection or cell-to-cell spreading; points out that herpesvirus gD protein binds HVEM and other cellular receptors through the same gD region; and states that one of skill in the art would expect administration of claimed compositions to be useful in achieving clinically beneficial results in treatment or prevention of HSV1 and HSV2 infections.

The Declaration has not been found persuasive. With respect to Exhibit 2 and the teachings of the specification regarding pharmaceutical compositions in general, the state of the art with respect to pharmaceutical compositions in general is not disputed. Exhibits 3 and 4 and the discussion concerning those exhibits is not seen to be directly relevant to the claimed compositions and their use to treat/prevent HSV infection, since

they deal with the natural ligand for a TNF receptor; no natural ligand for HVEM is instantly disclosed. The direct relevance of Exhibits 5 and 6 is not understood. While Exhibit 5 does report *in vivo* results, the results concern CD4 as a receptor for HIV-1; Applicant has established no basis for correlating CD4-HIV-1 results to HVEM-HSV results. Exhibit 6 concerns *in vitro* ICAM-1 and rhinovirus results; no basis is provided for correlating these results. While it may be so that recombinant HVEM would bind to and sequester HSV1 particles and prevent their binding to cellular HVEM and other cellular receptor, and that herpesvirus gD protein binds HVEM and other cellular receptors through the same gD region, these results were obtained *in vitro* and no basis has been established for extrapolating results obtained in this particular system to a reasonable expectation for success in achieving a beneficial result in treating human viral infections.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,303,336. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pharmaceutical compositions comprising HVEM polypeptide as instantly recited are not distinguished from the HVEM polypeptide itself as claimed in US Patent No. 6,303,336.

Applicant has expressed willingness to submit a terminal disclaimer when otherwise allowable subject matter is indicated.

The rejection is maintained as there is no reason to withdraw it at this time.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna C. Wortman, Ph.D. whose telephone number is

703-308-1032. The examiner can normally be reached on Monday-Thursday, 7:30-5:00 and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Donna C. Wortman, Ph.D.
Primary Examiner
Art Unit 1648

dcw
October 17, 2002